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wherein n is an integer from 2 to the general formula XXXIII wherein n is an integer from 2 to the general formula XXIIII wherein n is an integer from 2 to the general formula XXIIII wherein n is an integer from 2 to the general formula XXIIII not not not groups], and each Y is, independently, a peripheral moiety, [wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, and] wherein said mass-coded combinatorial library is produced by reacting a scaffold precursor having n reactive groups, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, with a peripheral moiety precursor subset selected from a peripheral moiety precursor set, said peripheral moiety precursor subset comprising a sufficient number of distinct peripheral moiety precursors such that there exist at least about 250 distinct combinations of n peripheral moieties derived from said peripheral moiety precursors, [wherein said subset includes at least two different peripheral moiety precursors that are each contacted with and can each react with at least two different reactive groups,] said method comprising the steps of:

- (a) contacting the <u>first</u> biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the biomolecule bind to the <u>first</u> biomolecule to form <u>first</u> biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the <u>first</u> biomolecule remain unbound;
- (b) separating the <u>first</u> biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;
- (c) dissociating the <u>first</u> biomolecule-ligand complexes; and
- (d) determining the molecular mass of each ligand to identify the set of n peripheral moieties present in each ligand;

wherein the molecular mass of each ligand corresponds to a set of n peripheral moieties present in that ligand, thereby identifying a member of the mass-coded combinatorial library which is a ligand for the <u>first</u> biomolecule.



52.

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(Amended) The method of claim 16, wherein all n reactive groups of the scaffold precursor are confacted with and can react with the same peripheral moiety precursor subset.

54. (Amended) The method of claim 16, further comprising the steps:

- (e) [contracting] contacting a second biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the second biomolecule bind to the second biomolecule to form second biomolecule-ligand complexes;
- (f) separating the second biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;
- (g) dissociating the second biomolecule-ligand complexes;
- (h) determining the molecular mass of each ligand for the second biomolecule; and
- (i) determining which molecular mass or masses determined in step (d) are not determined in step (h), thereby providing the molecular masses of members of the mass-coded combinatorial library which are ligands for the <u>first</u> biomolecule but are not ligands for the second biomolecule[.];

wherein each molecular mass determined in step (i) corresponds to a set of n peripheral moieties present in a ligand for the first biomolecule which is not a ligand for the second biomolecule, thereby identifying a member of the mass-coded combinatorial library which are ligands for the <u>first</u> biomolecule but are not ligands for the second biomolecule.

- 55. (*Amended*) The method of claim 54 wherein the <u>first</u> biomolecule and the second biomolecule are each, independently, a protein or a nucleic acid molecule.
- 56. (*Amended*) The method of claim 55 wherein the <u>first</u> biomolecule and the second biomolecule are each a protein, and the amino acid sequence of the second biomolecule is derived from the amino acid sequence of the <u>first</u>



biomolecule by insertion, deletion or substitution of one or more amino acid residues.

57.

(*Amended*) The method of claim 55 wherein the <u>first</u> biomolecule is a first protein and the second biomolecule is a second protein, said first and second proteins having the same amino acid sequence, wherein said first and second proteins have different posttranslational modifications.

- 59. (*Amended*) The method of claim 55 wherein the second biomolecule is a complex of the <u>first</u> biomolecule with a ligand.
- 60. (*Amended*) The method of claim 55 wherein the <u>first</u> biomolecule and the second biomolecule are each immobilized on a solid support.
- 62. (Amended) The method of claim 55, wherein one or [more] both of steps (b) and (f) is performed by contacting a solution comprising <u>first</u> biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion chromatography column, whereby the unbound members of the mass-coded combinatorial library elute from the column after the <u>first</u> biomolecule-ligand complexes or the second biomolecule-ligand complexes.

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- 63. (Amended) The method of claim 55, wherein one or both of steps (b) and (f) is performed by contacting a solution comprising <u>first</u> biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion [chromatography column] <u>membrane</u>, whereby the members of the mass-coded combinatorial library pass through said membrane and the <u>first</u> biomolecule-ligand complexes or second biomolecule-ligand complexes do not pass through said membrane.
- 64. (Amended) A method for identifying a member of a mass-coded combinatorial library which is a ligand for a first biomolecule but is not a ligand for a second biomolecule, said mass-coded combinatorial library comprising compounds of the general formula XY_n, wherein n is an integer from 2 to about 6, X is a scaffold

[having n reactive groups], and each Y is, independently, a peripheral moiety, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, and] wherein said mass-coded combinatorial library is produced by reacting a scaffold precursor having n reactive groups, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, with a peripheral moiety precursor subset selected from a peripheral moiety precursor set, said peripheral moiety precursor subset comprising a sufficient number of distinct peripheral moiety precursors such that there exist at least about 250 distinct combinations of n peripheral moieties derived from said peripheral moiety precursors, [wherein said subset includes at least two different peripheral moiety precursors that are each contacted with and can each react with at least two different reactive groups,] said method comprising the steps of:



- (a) contacting the second biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the second biomolecule bind to the second biomolecule to form second biomolecule-ligand complexes and members of the masscoded library which are not ligands for the second biomolecule remain unbound;
- (b) separating the second biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;
- (c) contacting the first biomolecule with the unbound members of the mass-coded combinatorial library of step (b), whereby members of the mass-coded combinatorial library which are ligands for the first biomolecule bind to the first biomolecule to form first biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the first biomolecule remain unbound;
- (d) dissociating the first biomolecule-ligand complexes;
- (e) determining the molecular mass of each ligand for the first biomolecule?

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88.

(Amended)

wherein each molecular mass determined in step (e) corresponds to a set of n peripheral moieties present in a ligand for the first biomolecule which is not a ligand for the second biomolecule, thereby identifying a member of the mass-coded combinatorial library which is a ligand for the <u>first biomolecule</u> but is not a ligand for the second biomolecule.

A method for identifying a member of a mass-coded combinatorial

library which is a first ligand for a biomolecule and binds the biomolecule at [the] a binding site of a known second ligand for the biomolecule, said mass-coded combinatorial library comprising compounds of the general formula XY_n, wherein [in] n is an integer from 2 to about 6, X is a scaffold [having n reactive groups], and each Y is, independently, a peripheral moiety, [wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, and] wherein said mass-coded combinatorial library is produced by reacting a scaffold precursor having n reactive groups, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to forma covalent bond, with a peripheral moiety precursor subset selected from a peripheral moiety precursor set, said peripheral moiety precursor subset comprising a sufficient number of distinct peripheral moiety precursors such that there exists at least about 250 distinct combinations of n peripheral moieties derived from said peripheral moiety precursors, [wherein said subset includes at least two different peripheral moiety precursors that are

a) contacting the biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the biomolecule bind to the biomolecule to form biomoleculeligand complexes and members of the mass-coded combinatorial library which are not ligands for the biomolecule remain unbound;

each contacted with and can each react with at least two different reactive

groups,] said method comprising the steps of:

